UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,991	04/13/2006	Lital Alfonta	54-000711US	2082

22798 7590 05/06/2009

QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.
P O BOX 458
ALAMEDA, CA 94501

EXAMINER	
GEBREYESUS, KAGNEW H	

ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
05/06/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,991	ALFONTA ET AL.	
	Examiner	Art Unit	
	KAGNEW H. GEBREYESUS	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *31,34,35,39,41-44 and 46-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31,34,35,39,41-44 and 46-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *4/7/2009* .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response on December 18, 2008 to the Office Action dated October 28, 2008 is acknowledged. Applicants have added claims 48-58. Claims have been amended. Claims 31, 34, 35, 39, 41-44, 46 and 47-58 are present for examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 46, 47-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims recite a composition comprising a protein and an ORS and/or an O-tRNA which can further comprise a nucleic acid comprising at least two selector codons. It is not clear if the O-RS/O-tRNA and the nucleic acid comprising selector codon(s) are used to produce the protein in the composition or if the protein is in the composition "*a priori*". For examination purposes the ORS aminoacylates the O-tRNA and the O-tRNA incorporates the unnatural amino acid(s) into the selector codon to produce the protein in the composition. Thus the composition comprises all the components. Clarification is required.

Maintained - Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 31, 34, 35, 39, 41-44, 46, 47, 48, 50-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz et al (US 7, 045,337 B2 / US 2003/0082575 A1 **in IDS**) in view of Rodriguez et al. for the reasons of record as set forth in the Office action mailed 10/28/2008.

Applicants argue:

".. Applicants traverse. A proper analysis under the recently reaffirmed *Graham v John Deere* standard demonstrates the non-obviousness of the invention. According to the Supreme Court in *KSR International Co v. Teleflex* (550 U.S. __ (2007); 127 S. Ct. 1727, 1740-41, 82 USPQ2d 1385-1396 (US 2007)), the appropriate standard for analyzing questions of obviousness is that: **the scope and content of the prior art are determined, differences between the prior art and the claims at issue are analyzed and the level of ordinary skill in the pertinent art is resolved**. Against this background the obviousness or non-obviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unresolved needs, failure of others, etc. might be utilized to give light to the circumstances surrounding the origin of the subject matter to be patented.

/d. quoting *Graham v. John Deere of Kansas City* 383 U.S. 1, 17-18.

Applicant's argument has been considered but not found persuasive. Claims 31, 34, 35, 39, 41-44, 46, 47, 48, 50-58 are obvious because Schultz et al teach incorporating various unnatural amino acids into proteins of interest. Page 8 column 2, line 46-67, page 17, column 1, line 46-48, page 33 under the title "Compositions that include Proteins with Unnatural Amino Acids" and through out the specification teach composition comprising a wide variety of proteins including therapeutic proteins, diagnostic proteins and industrial proteins comprising one or

more unnatural amino acids (see for e.g. pages 35-36). In one aspect of Schultz et al's invention, the protein comprises the unnatural redox-active amino acid 3, 4-hydroxy-L-phenylalanine (DHP) (see figure 17, page 28). Furthermore Schultz et al in fig. 29 show additional unnatural redox active amino acids (e.g. #64, #41). Paragraph [0318] of Schultz et al teaches expressing myoglobin comprising a desired unnatural amino acid (claims 39, 40). Paragraph [0245] of Schultz et al teaches pharmaceutical compositions comprising a protein comprising a desired unnatural amino acid. Paragraph [0048] of Schultz et al teaches one or more unnatural amino acids can be incorporated in the protein (claim 38).

Schultz et al do not specifically teach a protein composition comprising at least two or more different redox active amino acids including those selected from the group consisting of: a 3,4-dihydroxy-L-phenyalanine (DHP), a 3,4,5-trihydroxy-L-phenylalanine, a 3-nitro-tyrosine, a 4-nitro-phenylalanine, and a 3-thiol-tyrosine.

However Schultz et al contemplate producing proteins comprising any unnatural amino acid or redox active unnatural amino acids including at least 3, 4-dihydroxy-L-phenyalanine (DHP) (see figure 17, page 28), a 3-nitro-tyrosine (S76 in fig. 29), and a 4-nitro-phenylalanine (see fig. 26, 4th molecule). Schultz et al do not specifically teach a protein comprising two redox active unnatural amino acids *per se*.

Rodriguez et al show that the redox active unnatural amino acid 3, 4-hydroxy-L-phenylalanine (DHP) can be incorporated into a protein in such a way as to exclude the incorporation of L-tyrosine. Rodriguez et al do not teach incorporation of other redox active unnatural amino acids.

One of ordinary skill would have a reasonable expectation of success in producing proteins comprising two or more different redox active amino acids because Schultz et al teach the overall strategy for incorporating unnatural amino acids including 3, 4-dihydroxy-L-phenyalanine (DHP) (see figure 17, page 28), a 3-nitro-tyrosine (S76 in fig. 29), and a 4-nitro-phenylalanine (see fig. 26, 4th molecule) disclosed in Schultz et al.

Claims 31, 33-43 drawn to compositions comprising a protein that comprises two or more different redox active amino acids including the redox-active amino acids 3, 4-hydroxy-L-phenylalanine (DHP) are obvious over Schultz et al. in view of Rodriguez et al because Rodriguez et al teach that 3, 4-hydroxy-L-phenylalanine (DHP) can be incorporated into a protein. The embodiments in claims 41, 42 and 44 which recites that the protein is capable of undergoing oxidation, or being a redox catalyst are inherent to the redox-active unnatural amino acid incorporated into a protein.

The scope and content of the prior art (specifically Schultz et al (US 7, 045,337 B2) has sufficient teachings regarding proteins comprising unnatural amino acids. Furthermore while Schultz et al (US 7, 045,337 B2) do not recite every embodiment individually, in light of the teachings in the specification of Schultz et al and claims 1-6 that specifically recite cells comprising OtRNA, ORS and nucleic acid (mRNA) encoding a protein of interest (claim 1) and the unnatural amino acid 3, 4, dihydroxy-phenyl alanine, (claim 6), a person of ordinary skill in the art would be able to clearly envisage a protein comprising at least one or more 3, 4, dihydroxy-phenyl alanine or any redox active amino acids disclosed in Schultz et al (3,4-dihydroxy-L-phenyalanine (DHP) (see figure 17, page 28), a 3-nitro-tyrosine (S76 in fig. 29),

and a 4-nitro-phenylalanine (see fig. 26, 4th molecule)). **Also note that the instant application does not teach other redox-active unnatural amino acids incorporated into proteins.**

Applicants further argue:

The current Examination Guidelines (e.g., MPEP 2143) and *KSR* require the Office in an obviousness rejection to provide a statement as to why one of skill would have combined known elements. Further, an obviousness rejection must include fact-based findings demonstrating: 1) a combination of reference elements describing each limitation of the claims, 2) known elements that function in the same way in the combination as in the references themselves, 3) the elements are combined by known methods, 4) the result of the suggested combination of elements would have been predictable, and 5) one of skill in the art would have expected success in providing the claim in light of the references. Here, the rejection fails each of these requirements, as applied to the *Graham* factors.

The Action alleges the existence of unnatural redox amino acids in the context of the orthogonal translation system components of Schultz '337. Rodriguez describes a rat brain soluble fraction that may inexplicably incorporate at most a single DHP to the C- terminus of a peptide. The Action does not state a finding of facts, required by MPEP 2143, explaining how the combination of elements would be obvious to one of skill based on the cited references…"

However the Rodriguez reference only demonstrates that proteins comprising 3, 4, dihydroxy-phenyl alanine in place of a tyrosine can be produced naturally. Furthermore while Schultz et al does not specifically recite a composition comprising a protein comprising all the redox unnatural amino acids (3,4,5-trihydroxy-L-phenylalanine, 3-nitro-tyrosine, 4-nitro-phenylalanine, and a 3-thiol-tyrosine), Schultz et al does teach cells comprising the components required to produce a protein comprising at least 3, 4, dihydroxy-phenyl alanine (DHP) among the redox active amino acids recited in the instant application.

Furthermore to produce the protein composition claimed in the instant application, Applicants used a screening procedure and identified the ORS/OtRNA pair that can incorporate 3, 4-dihydroxy-L-phenylalanine. Applicants disclose a myoglobin protein comprising a single redox-active amino acid, namely 3, 4-dihydroxy-L-phenylalanine (DHP or L-DOPA) as a

working example (note that other redox-active unnatural amino acids incorporated in proteins are not specifically taught in the instant application).

Based on the above teaching which can serves as proof of principle for incorporating a redox-amino acid in a protein, Applicants claim a protein comprising at least one or at least two redox-active unnatural amino acids selected from 3, 4-dihydroxy-L-phenylalanine, a 3, 4, 5-trihydroxy-L-phenylalanine, a 3-nitro-tyrosine, a 4-nitro-phenylalanine and a 3-thiol-tyrosine in claims 31 and dependent claims 47-58. The ORS molecules with 90% sequence identity recited in claims 47 or the ORS molecules from any source with no sequence disclosure recited in claims 57 are encompassed in Schultz et al because most of the ORS disclosed in Schultz et al are within this limitation (See for example SEQ ID NO: 51, 53, 54, 55, 61...of Schultz et al which are all above 90%). Therefore the rejection of claims 46, 47, 48, 50-58 as obvious over Schultz et al in view of Rodriguez et al. is maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 31, 46, 47, 48, 50-58 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim1-6, 14 and15 of U.S. Patent No. 7,045337. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-6, 14 and 15 are drawn to cells comprising an ORS and an OtRNA, unnatural amino acids including the redox active 3 DHP (see claim 6) in the presence of an mRNA that produces the protein of interest (see claim 1 and 4). Claims 47, 48, 50-58 encompass a composition comprising an ORS, OtRNA and a nucleic acid with two selector codons (claim 58). Given that claims 46, 47-58 of the instant application are drawn to a protein produced in a composition comprising an ORS, OtRNA, the redox unnatural amino acid(s) and the nucleic acid of interest as suggested in the 35 U.S.C. 112, second paragraph rejection above, these claims are obvious variants of the cells comprising an O-tRNA, O-RS, nucleic acid encoding the protein of interest and the unnatural amino acid composition claimed in claims 1-6, 14 and 15 of Schultz et al. (US 7,045,337).

Conclusion:

No claims are allowed..

This is a non-final action because the double patenting rejection was not made in the previous Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KAGNEW H. GEBREYESUS whose telephone number is (571)272-2937. The examiner can normally be reached on 8:30am-5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANDREW WANG can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kagnew H Gebreyesus/
Examiner, Art Unit 1656
4/28/2009

/Andrew Wang/
Supervisory Patent Examiner, Art Unit 1656

Formatted: Font: Not Bold